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NIH REQUEST FOR INFORMATION:

Input into the Scientific Strategic Plan for the Proposed National Institute of Substance Use and Addiction Disorders

ANALYSIS OF PUBLIC COMMENTS

OCTOBER 10, 2012

This report includes an analysis of the comments received through the NIH Request for Information (RFI): Input into the Scientific Strategic Plan for the Proposed National Institute of Substance Use and Addiction Disorders (NOT-OD-12-045)

Executive Summary

In 2010, the Scientific Management Review Board (SMRB), a congressionally-mandated oversight group, recommended that the National Institutes of Health (NIH) establish a new institute focused on addiction-related research and public health initiatives. In response, NIH proposed to create a new institute, with the working name of the National Institute of Substance Use and Addiction Disorders (NISUAD). A strategic planning committee, which includes individuals from potentially affected institutes and centers, is developing a draft scientific strategic plan to address scientific opportunities in substance use, abuse, and addiction research to: assist in meeting public health needs and improve training options for new investigators.

As part of the strategic planning process, the committee gathered input from the extramural community through a request for information (RFI) entitled, "Input into the Scientific Plan for the proposed National Institute of Substance Use and Addiction Disorders"[1]. The committee identified 13 issues in the RFI as important to consider as possible areas of research within the newly formed institute. Respondents were asked to reflect and comment on those 13 areas of research as they responded to the following questions:

1. For any of the areas identified above and any other specific areas you believe are worthy of consideration by NIH, please identify the critical issue(s) and effect(s) on the public, on scientists, or both.
2. Please identify and explain which of the issues you identified are, in your opinion, the most important for NIH to address and why.

Ripple Effect Communications, Inc. was contracted to provide third party analysis of the comments received through the RFI. This report provides an analysis of the 500 submissions received in response to the RFI.

DATA AND METHODS

Of the 500 submissions received, 470 were unique and responsive. The majority of submissions (80%) were from individuals; organizations provided the remaining 20%. We parsed each submission into a total of 1013 individual comments and developed a coding scheme to categorize comments into themes. In addition to coding the comments using themes, we also noted when respondents considered their issues a priority for the new institute.

Coding Scheme

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[1] http://grants.nih.gov/grants/guide/notice-files/NOT-OD-12-045.html

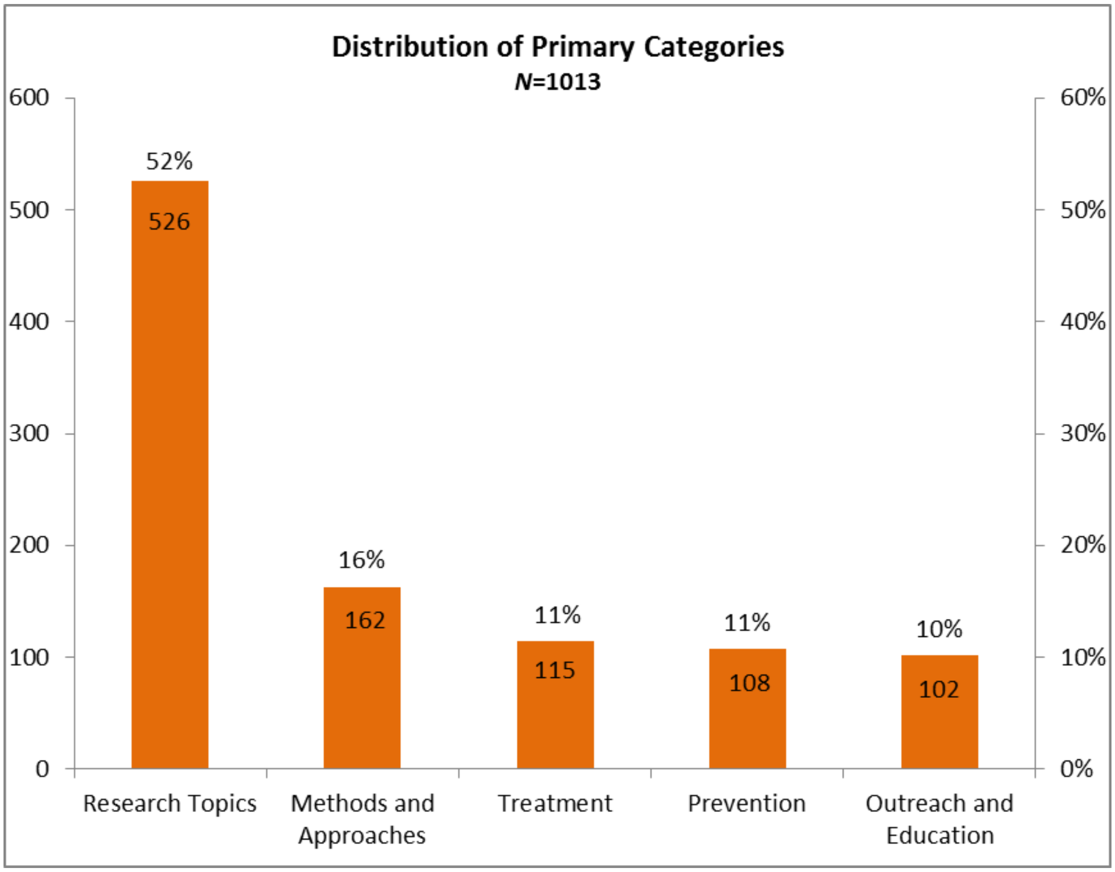
The 13 areas of research offered by the committee provided the conceptual foundation for our coding scheme, which team members further developed using an iterative, grounded theory approach. Conceptually, we organized all ideas (areas of research identified by the committee *and* respondents) into five primary categories:

- Research Topics
- Methods and Approaches
- Treatment
- Prevention
- Outreach and Education

Within each primary category, we identified themes. Of the original 13 areas of research identified by the committee, six became themes and seven were integrated into broader themes. The final coding scheme consisted of five primary categories and 17 themes.

FINDINGS

All frequency distributions throughout this report are calculated using the total number of comments extracted (*N*=1013, 100%). Of the five primary categories, the greatest number of comments were captured under *Research Topics* (*n*=526, 52%).



The distribution of comments across the total data set was almost identical to the distribution of comments across the priority sub-set, and the top five themes identified as priority were the same as the five most frequently coded themes. The top five themes identified as a priority were *Alcohol Use and Addiction, Antecedents and Comorbidity, Other Addictions or Drugs of Abuse, Broaden the Approach,* and *Develop and Evaluate Interventions and Treatments*. Of 470 respondents, 431 identified at least one issue as a priority.

Top Five Themes Identified as Priority

1. *Alcohol Use and Addiction*
2. *Antecedents and Comorbidity*
3. *Other Addictions or Drugs of Abuse*
4. *Broaden the Approach*
5. *Develop and Evaluate Interventions and Treatments*

CONCLUSIONS

More than half of the comments from respondents to this RFI suggested research topics that should be included in the scientific strategic plan for the proposed National Institute of Substance Use and Addiction Disorders. Alcohol consumption and the causes and developmental progression of addiction were the two most commonly identified areas of research. Collectively, the other half of the comments suggested the new institute give greater organizational support to all issues related to treatment, prevention and outreach and education. A group of respondents also suggested the need for improved methods and research designs, with greater emphasis on the practical applications of new knowledge.

Substance use, abuse and addiction were broadly recognized as complex and multi-faceted public health issues. Concerned about reducing the public health burden, respondents called for a better balance between support for biological and biomedical studies versus behavioral and psychosocial investigations. Often, it was suggested that the allocation of funding should match the public health burden of the identified research problem. Regardless of the area of research, a common message that cut across themes was the need for inter- and multidisciplinary research that recognized use, abuse, and addiction as a developmental problem with a complicated set of influences and outcomes. In the context of the NIH mission, and pointing to the high economic and social costs of substance use, abuse, and addiction at the individual, family, community levels and beyond, respondents urged the NIH to support all efforts toward tangible outcomes with direct and positive influences.

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Background

NIH REQUEST FOR INFORMATION

Established under the NIH Reform Act of 2006, the Scientific Management Review Board (SMRB) advises the NIH director on the use of certain organizational authorities reaffirmed under the same act. In April 2009, the SMRB formed the Substance Use, Abuse, and Addiction Working Group to provide recommendations to the full SMRB regarding whether organizational change within NIH could further optimize research into substance use, abuse, and addiction, and maximize human health and/or patient well-being[2]. Based on the recommendations of the working group, the SMRB in 2010 recommended that NIH dissolve the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the National Institute on Drug Abuse (NIDA) and form a single institute focused on substance use, abuse and addiction. After extensive consideration, the NIH agreed with the SMRB recommendation regarding the potential opportunities that a single institute would afford, and a strategic planning committee was formed to develop a scientific strategic plan for the proposed institute.

To help inform its deliberations, the committee published a request for information (RFI) entitled, "Input into the Scientific Strategic Plan for the proposed National Institute of Substance Use and Addiction Disorders"[3]. As the planning committee sought to gather input from extramural and intramural researchers, academic institutions, industry, and the public, they identified 13 potential areas of research as opportunities and asked responders to consider them as they developed their submissions.

- Developing a compendium of the pharmacokinetic and pharmacodynamic interactions between alcohol and the therapeutics used to treat general medical and psychiatric conditions (e.g., hypertension, diabetes, epilepsy, depression);
- Encouraging research on the generation of novel metabolites resulting from the *in situ* interaction of alcohol with opiates, stimulants, hallucinogens, or inhalants (e.g., the production of cocaethylene when alcohol and cocaine are co-ingested) and their pharmacokinetic and pharmacodynamic properties and toxicity;
- Understanding the mechanisms by which alcohol and other drugs of abuse increase risk for certain diseases (e.g., cancers), particularly when used in combination;
- Developing strategies to enhance stakeholder interest in developing medications to treat various addictions, including nicotine and alcohol;
- Engaging the medical community in prevention and treatment of drug addiction and alcoholism;
- Encouraging patient recognition and utilization of effective substance abuse treatments;
- Alleviating the translational bottleneck for treatments to move from the bench to the bedside to the community;

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[2] http://smrb.od.nih.gov/working_groups/suaa-charge

[3] http://grants.nih.gov/grants/guide/notice-files/NOT-OD-12-045.html

- Improving prevention efforts by developing a better understanding of the patterns and trajectories of drugs of abuse and their influence on brain development;
- Designing clinical trials that accurately reflect real-world conditions (e.g., greater inclusion of polydrug users);
- Encouraging research to elucidate the impact of using one substance (e.g., alcohol) on likelihood of relapse to other substances (e.g., other drugs);
- Targeting efforts to prevent substance abuse in adolescents and young-adults;
- Understanding the implications of Policy Research on substance use patterns and trajectories, especially in youth; and,
- Furthering knowledge of tobacco use and addiction, including comorbidity with other addiction and psychiatric disorders.

Respondents were asked to consider these 13 areas of research as they responded to two questions:

1. For any of the areas identified above and any other specific areas you believe are worthy of consideration by NIH, please identify the critical issue(s) and effect(s) on the public, on scientists, or both.
2. Please identify and explain which of the issues you identified are, in your opinion, the most important for NIH to address and why.

A total of 500 submissions were received through the online submission process, which was open from February 8, 2012 through May 11, 2012. This report is an analysis and summary of the public comments and serves as a tool for the planning committee as it develops a strategic plan for research for the proposed National Institute of Substance Use and Addiction Disorders (NISUAD, working title).

THE ROLE OF RIPPLE EFFECT COMMUNICATIONS, INC.

Ripple Effect Communications, Inc. was engaged by the NIH Office of the Director to perform an analysis of the data received through the RFI. As an independent contractor, Ripple Effect staff is not invested in the planning committee deliberations and, therefore, has no bias toward the outcomes of the assessment. However, Ripple Effect is uniquely positioned to bring a continuum of working knowledge and expertise about NIH to the analysis process. Our staff's diverse levels of knowledge about NIH allow an open interpretation of respondents' thoughts and ideas, which ensures full expression but also provides accurate context for understanding potentially complicated messages.

Methods

We used both quantitative and qualitative research methods as part of the analysis process. While focusing on and maintaining the integrity of the areas of research identified by the planning committee, we remained open to the data. We used grounded theory coding and analysis methods to capture ideas from respondents that went beyond those identified by the planning committee and were pervasive enough to warrant their own theme.

Of the 500 submissions received, 470 were unique and responsive. The majority of respondents chose “self” as affiliation (*n*=377; 80%), the rest identified as affiliated with an “organization” (*n*=93, 20%).

ANALYSIS PROCESS

All submissions were uploaded and organized into a central SharePoint database. The contents of each individual submission (self or organization) were extracted into multiple comments and coded according to the coding scheme. All areas of research identified by the planning committee were quantified as part of the coding process, and tallies are presented in Appendix A. A total of 1013 comments were parsed and analyzed using both SharePoint and Excel. Except for those involving priority comments, all calculations provided in this report are based on the overall number of comments extracted: *N*=1013.

Coding Scheme

We began the process of iterative code development using the 13 areas of research originally identified by the planning committee. After studying the data, it became clear that different levels of conceptual organization and coding would be necessary; respondents often described their ideas for research in broader terms than those put forth by the committee. With the goal of maintaining the integrity of the planning committee’s areas of research, six became themes and seven were integrated into broader themes. The final coding scheme consisted of five primary categories and 17 themes (see Appendix B for the full coding scheme). Below is an organizational table that illustrates which themes are the planning committee’s areas of research (*), which are an integration of ideas (+, ɫ), and which are strictly data-driven (no symbol).

Primary Category	Theme
Research Topics	Alcohol Use and Addictionɫ Tobacco Use and Addiction+ Other Addictions or Drugs of Abuse Increased Risk of Disease+ Antecedents and Comorbidity
Methods and Approaches	Broaden the Approach Research Methods+

Primary Category	Theme
	Policy Research*
Treatment	Remove Barriers to Access+ Develop and Evaluate Interventions and Treatments+ Relapse and Recovery+
Prevention	General Prevention Research Brain Development* Targeted Early Prevention*
Outreach and Education	Strategies for Drug Development* Workforce Training and Development+ Public Outreach and Education

*Committee-identified area of research

+Includes one committee-identified area of research

ǂ Includes two committee-identified areas of research

Priority

To assess the priority of respondents' comments, we created a sub-group of data that met at least one of the following criteria:

1) The comment was included in response to question two from the RFI, "Please identify and explain which of the issues you identified are, in your opinion, the *most important* for the Working Group to address and why."
2) The respondents explicitly expressed priority by using priority language, such as "critical," "important," or "essential," etc.

If no priority was indicated or if the respondents explicitly expressed that the item was NOT a priority, the comment was not included as part of the priority analysis.

We analyzed both the number of comments coded as priority (*n*=847, 84%), and also the number of people who identified at least one theme as a priority (*n*=431, 92%). Analysis of priority is presented in section two of the Findings portion of the report below. From the individual perspective, priority is presented in table format and ordered based on the frequency with which each person identified a theme (the presentation is not as a mathematical rank order).

Findings

Findings are divided into two major sections corresponding to the questions posed in the RFI. Section one includes analysis of the comments received in response to question 1: “For any of the areas identified above and any other specific areas you believe are worthy of consideration by NIH, please identify the critical issues(s) and effect(s) on the public, on scientists, or both.” First, we provide a quantitative overview of the primary categories and include a breakdown by affiliation, and then we provide a detailed qualitative analysis of the 17 themes.

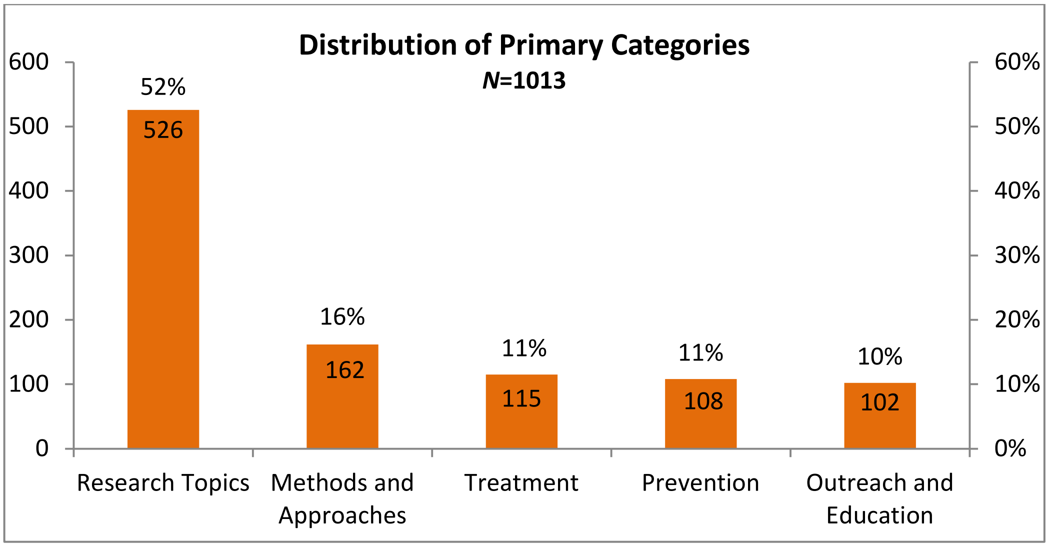
Section two addresses question 2: “Please identify and explain which of the issues you identified are, in your opinion, the most important for NIH to address and why.” We created a sub-set of data composed of comments where respondents explicitly identified their comment as a priority. We quantified the sub-set, conducted a comparative analysis with the overall data set, and then from an individual perspective, ordered the 17 themes by priority.

SECTION ONE: ANALYSIS OF COMMENTS

We parsed the 470 responsive, non-duplicate submissions into 1013 individual comments. Each comment received one code corresponding to one theme. The codes were quantified and analyzed for both frequency of use and content. This section includes a quantitative overview of the primary categories, and a comprehensive examination of the themes.

An Overview of Primary Categories

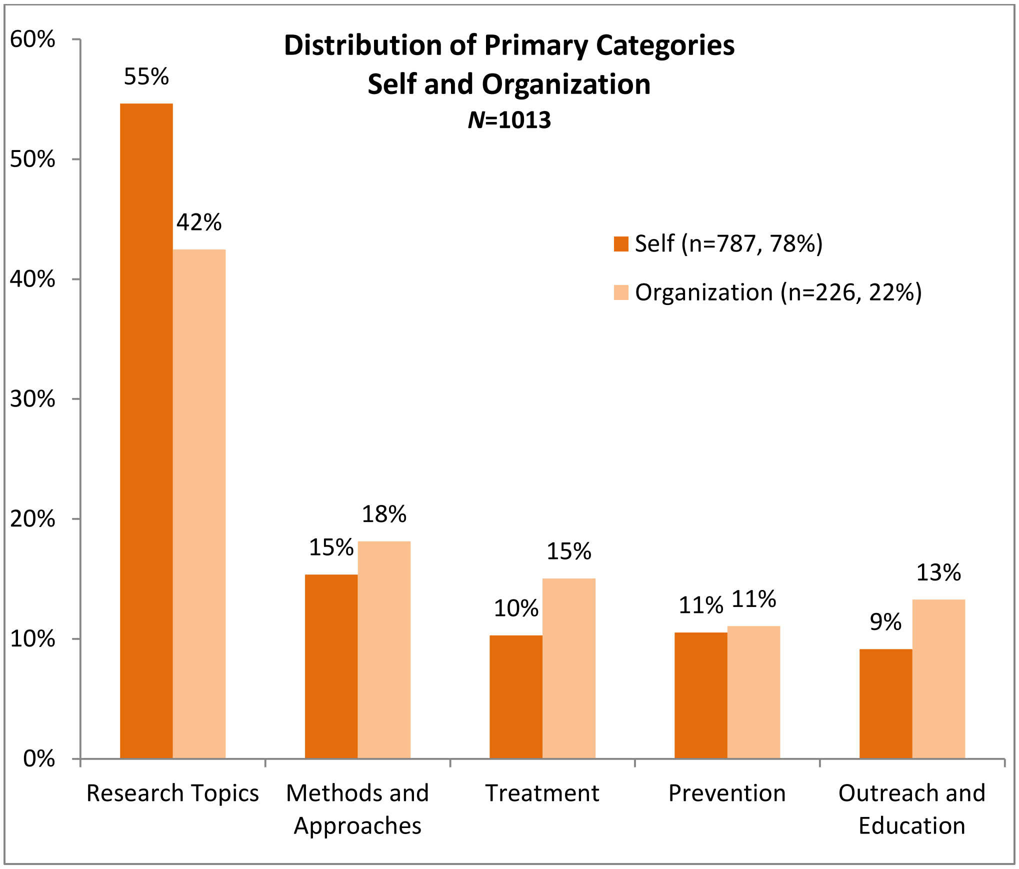
The committee’s 13 areas of research were integrated into a coding scheme that gave voice to ideas that went beyond those identified in the RFI. In total, there were five primary categories (broad and overarching concepts) and 17 themes (more specific ideas).



The majority of comments fell under the primary category *Research Topics* (5 themes, *n*=526; 52%). This category contained the greatest number of themes, as respondents proposed a number of ideas for research. The remaining comments fell into the four other primary categories: *Methods and Approaches* (3 themes, *n*=162, 16%), *Treatment* (3 themes, *n*=115; 11%), *Prevention* (3 themes, *n*=108; 11%), and *Outreach and Education* (3 themes, *n*=102; 10%). The primary categories *Treatment* and *Prevention* included research related suggestions, but were grouped separately from *Research Topics* because of the dynamic nature of the data, and to provide a more accessible and nuanced analysis. Often, respondents noted that the new institute could do more than support research; it could also provide organizational support in the form of leadership (e.g., setting public health goals and liaising with other federal agencies) and information dissemination (e.g., best practices and population level statistics).

Primary Categories by Respondent Affiliation

Respondents (*n*=470) self-identified with one of two types of affiliation: as an independent individual (self: *n*=377, 80%) or on behalf of an organization (organization: *n*=93, 20%). Of the total comments extracted, 787 (78%) were from those who identified as “self,” and 226 (22%) were from those who identified as “organization.”



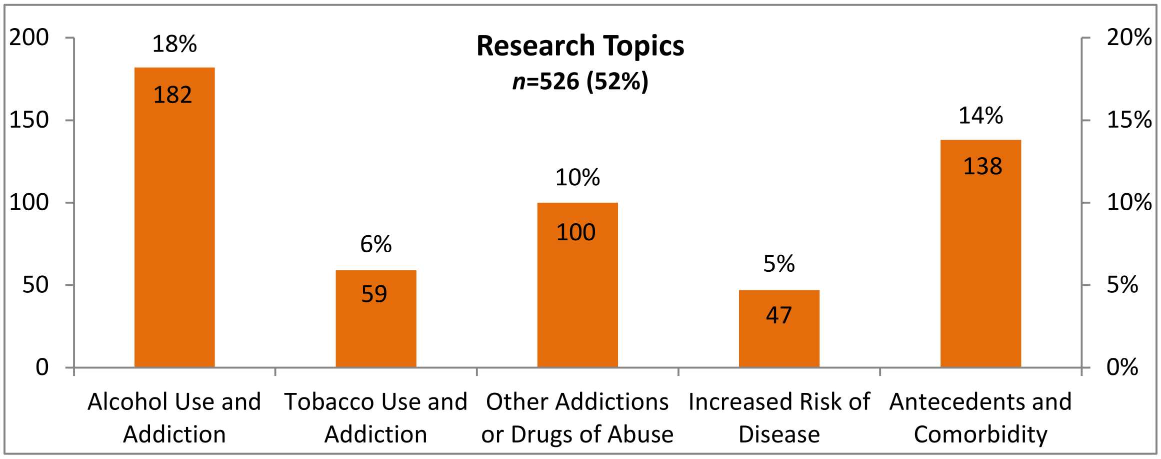
Regardless of affiliation, respondents most often suggested *Research Topics*. However, those who identified as an organization more frequently mentioned ideas related to *Methods and Approaches*, *Treatment,* and *Outreach and Education* compared to individuals.

Analysis of Themes

The 17 themes are presented and discussed here in detail. From the original 13 areas of research identified by the committee, six became themes and seven were integrated into broader themes (e.g., the original issue *Real-World Clinical Trials* became a part of the data-driven theme, *Research Methods)*; five themes were strictly data driven. The title and full description of the themes is provided in Appendix B. A graph summarizing the frequency distribution of the total comments across themes is provided in Appendix C.

Research Topics (Primary Category 1)

The majority of comments fell within the *Research Topics* primary category (*n*=526; 52%), which captured areas of research, or portfolios, that respondents deemed important and necessary to include within the new institute. Three-quarters of the comments within this primary category fell into one of these three themes: *Alcohol Use and Addiction*, *Antecedents and Comorbidity*, and *Other Addictions or Drugs of Abuse*.



Alcohol Use and Addiction (Theme 1)

All comments that mentioned alcohol use, abuse, and addiction were coded within *Alcohol Use and Addiction* (*n*=182, 18%), which integrated two of the committee's original areas of research (below) with ideas that emerged from the data.

- Encouraging research on the generation of novel metabolites resulting from the *in situ* interaction of alcohol with opiates, stimulants, hallucinogens, or inhalants (e.g., the production of cocaethylene when alcohol and cocaine are co-ingested) and their pharmacokinetic and pharmacodynamic properties and toxicity

- Developing a compendium of the pharmacokinetic and pharmacodynamics interactions between alcohol and the therapeutics used to treat general medical and psychiatric conditions (e.g., hypertension, diabetes, epilepsy, depression)

Generally, comments coded with *Alcohol Use and Addiction* referred to alcohol addiction as a major health problem with severe economic and social costs. As a legal substance that is used recreationally and often recommended in moderation for positive health benefits, respondents suggested alcohol was the most important substance, if not the only substance, that should be studied. Within the *Alcohol Use and Addiction* theme, we identified the following sub-themes:

- Physiological Effects of Alcohol
- Interaction Issues
- Fetal Alcohol Spectrum Disorders
- Broaden Alcohol Research

Physiological Effects of Alcohol. Respondents specifically requested that NIH avoid splitting studies on the physiological effects of alcohol and keep all aspects of such research in the new institute. Several individuals noted the impact of alcohol on many organ systems in the body and emphasized the importance of keeping a focused research plan. Serious concern was expressed about the priority that alcohol-related portfolios would receive if they were moved to disease-specific institutes.

> *Having sat on the relevant study section for this type of work (GMPB), I was struck that studies involving pathophysiological responses to alcohol were clearly viewed as not being at the same level of importance as other conditions, probably because alcohol consumption is by in large a voluntary activity, whereas the induction of most other GI conditions is not. My worry is that basic pathophysiology studies of the effects of alcohol will be a very low priority for NIDDK.* (#118)

The liver and brain were two organ-specific areas of research frequently mentioned. Respondents interested in liver function stated there wasn't enough knowledge about alcohol-induced liver disease and requested support for research and treatments to reduce the high rates of morbidity and mortality. Also important to respondents was research about the developmental effects of alcohol on the brain and central nervous system, and the impact of alcohol on cancer and HIV/AIDS.

Interaction Issues. Most commonly, alcohol was perceived as relatively benign on its own; however, respondents were concerned about the negative effects of alcohol when used in combination with other drugs of abuse or therapeutics. Respondents raised concerns about complications from alcohol-containing medications administered as therapeutics to alcohol users who need treatment for general medical or psychiatric conditions; one respondent mentioned that some over-the-counter drugs contain 3-26% alcohol. Another respondent pointed to poly-drug use and reminded NIH about the complications that arise with treatment plans and therapies identified to work on a single drug of abuse. Those concerned about the issue of driving under the influence suggested investigating the influence of interactions between alcohol and other drugs of abuse related to the outcomes of operating motor vehicles.

Fetal Alcohol Spectrum Disorders. All respondents concerned about Fetal Alcohol Spectrum Disorders (FASD) requested that NIH continue its substantial focus on FASD. The main concern was the location of FASD research portfolios; all but one of the comments advocated the inclusion of all FASD research in the new institute. Most respondents felt that moving some FASD investigations to different institutes (e.g., NICHD) would be detrimental to the field. The primary reason expressed for keeping all FASD research together in the new institute was the conviction that strong benefits would result from the synergies of having all research relating to alcohol use, abuse, and addiction within one institute.

Respondents questioned how research could be divided, pointing to the unique nature of FASD, and the involvement of both the developing child and the mother. They stated that separating this unit would be artificial. Respondents asserted that the study of the developmental effects of alcohol could not be divided at any logical point between fetal development and other stages of life when alcohol influences the brain and other organ systems. Fetal development is just the beginning of a continuum.

Specific suggestions for research included:

- Studying how the early developmental effects of alcohol exposure influence later stages of life; FASD infants and children have a much greater tendency toward alcohol abuse and addiction problems as teenagers and adults;
- Grouping the possible epigenetic effects from early exposure to alcohol with other studies about how alcohol affects genes and gene expression; and
- Supporting a “systems biology approach” for studying alcohol effects on the many organ systems and at all levels of research (basic, translational, prevention, treatment/intervention).

Beyond research, respondents were adamant that promoting FASD prevention, especially programs directed toward young women and binge drinking, could not logically be separated from studies of how alcohol influences the developing brain.

Broaden Alcohol Research. Because many individuals can use alcohol responsibly, and because evidence demonstrates potential health benefits when used in moderation, respondents suggested a need for research from a developmental perspective.

> *Not everyone who drinks alcohol will become an alcoholic. Through an unknown combination of genes, environment and development, some people will ultimately become problem drinkers, while others can drink responsibly throughout their lives. In my opinion, it will be through focused efforts on developmental alcohol research that we gain more insight into the real factors contributing to an individual’s development of alcohol abuse/dependence.* (#417)

Emphasizing alcohol consumption as a continuum, respondents suggested that taking a broader approach would bring attention to additional patterns of drinking beyond addiction. There was a call for more studies to investigate the beneficial or negative effects of low and moderate drinking, and also a call for more studies on binge drinking. One respondent suggested research to identify the social, psychological, and biological factors associated with binge drinking, including the influence of gender.

Tobacco Use and Addiction (Theme 2)

Tobacco Use and Addiction (*n*=59, 6%) included the following committee-identified area of research:

- Furthering knowledge of tobacco use and addiction, including comorbidity with other addiction and psychiatric disorders.

Respondents who spoke to the overall theme of *Tobacco Use and Addiction* stressed tobacco use as one of the country's top public health issues. Respondents were adamant that all research related to tobacco be included in the new institute. To gain a better understanding of tobacco-related dependency and addiction (therefore leading to better treatment options), one respondent suggested additional research to understand the complex relationship between smoking behaviors and the chemical addiction.

> *Some research suggests that smoking addiction is much more complex than chemical dependency on nicotine. In the first place, smoke may contain additional chemicals that make it more addictive than non-combusted tobacco and more addictive than nicotine itself. In the second place, there is reason to believe that people may become addicted to the motions of the act of smoking and to the visual manifestation of smoke.* (#196)

Respondents felt more should be done to reduce tobacco use and addiction, and they advocated a focus on prevention research targeting young people. Two issues repeatedly called to attention were: the need to understand the role of tobacco use in connection to subsequent experiments with other drugs and alcohol; and the perception that quitting tobacco would have a negative impact on weight.

Within the *Tobacco Use and Addition* theme, we identified two sub-themes:
- Tobacco Use and Comorbidity
- Behavioral Interventions

Tobacco Use and Comorbidity. Recognizing the high comorbidity of tobacco addiction with alcohol and other drugs and psychiatric disorders, respondents supported this area of research originally identified by the committee.

> *Tobacco use is highly comorbid with alcohol use, and therefore all research related to tobacco should be housed within the new institute, to better serve public health. In particular, prevention and treatment of tobacco use disorder should be included in the portfolio of the new institute, to maintain and promote research synergies.* (#180)

Respondents believed tobacco and alcohol share common features (e.g., both are legal substances often used in social settings), leading to high comorbidity. The combined use of tobacco and alcohol was noted as having a collective and negative impact on individuals that results in severe medical outcomes.

> *Smoking is an additive risk factor for development of hepatocellular carcinoma in patients with chronic viral hepatitis or liver disease due to alcohol. There is also a marked increase in oropharyngeal cancers in patients with alcohol abuse who smoke.* (#246)

While the physical health effects of comorbid use of tobacco and alcohol are well known, the psychosocial outcomes are rarely discussed; respondents encouraged NIH to support future studies focused on behavioral issues.

Behavioral Interventions. This data-driven issue captured comments related to the development and delivery of more effective behavioral interventions to reduce tobacco use. There were calls for research to address new treatment options because individuals respond differently to current treatments and therapy. Despite advances in replacing tobacco with less hazardous nicotine sources and the development of drugs targeting neuronal receptors, the limited success of available treatments was perceived as a major reason why tobacco is still the leading cause of preventable mortality and morbidity. Two critical questions were cited: “How to help people quit?” and “Why are some people more successful at quitting than others?” While continued medical research is warranted, respondents frequently emphasized behavioral interventions.

> *While there has been innovation in pharmacotherapy for smoking cessation in the last 20 years, there has been little innovation in psychosocial smoking cessation treatments (#4).*

To solve tobacco addiction, respondents emphasized how critical it is to understand human behavior, and more importantly, how to effectively change it.

Other Addictions or Drugs of Abuse (Theme 3)

Beyond alcohol or tobacco, this data-driven theme, *Other Addictions or Drugs of Abuse,* captured comments (*n*=100, 10%) related to the use, abuse, and addiction to other substances or problem behaviors. This theme included five additional topics not included in the original 13 areas of research.

- Illegal Substance Abuse
- Prescription Medication Abuse
- Food Addiction
- Pathological Gambling
- Addiction to Sex

Illegal drug use and behavioral addictions were most frequently mentioned; caffeine and over-the-counter drugs were infrequently mentioned, but cited as addictive substances that also warranted inclusion in the new institute.

Illegal Substance Abuse. Comments about illegal substance abuse were often mentioned in the context of the negative impacts they had on families and communities (including injury, crime and violence). Respondents encouraged research on medical consequences, non-pharmaceutical treatment options, and other alternatives to help reduce or eliminate illegal drugs in the community.

> *Therefore, there cannot be a better opportunity under the new NIH institute for the creation of a well-designed, comprehensive "consortium level" coalition of university academicians to engage in and design multipronged approaches aimed at identifying viable alternatives to reduce or eliminate illicit drug related harm [IDRH] globally.* (#92)

Respondents viewed the creation of this new institute as an opportunity for NIH to become more involved with the issues related to illegal drug use. Through the new institute, respondents encourage NIH to reach out to, and work with other federal agencies involved with the criminal justice system (e.g., the National Institute of Justice), as a means for efficiently identifying methods of treatment, intervention and prevention.

Prescription Medication Abuse. Becoming addicted to prescription drugs was perceived as a major public health problem that requires significant attention. One respondent cited a report of more than 14,000 fatal overdoses per year involving prescription opioids. Respondents pointed to the need to understand the risk factors for, and implications of, prescription drug abuse, specifically in relationship to chronic pain. With an eye toward strategies and interventions to reduce abuse, one suggestion for research included studying the effects of prescription drugs on brain responses in the presence and absence of pain.

> *Chronic pain affects more people than cancer, heart disease, and diabetes combined yet receives far less funding for research. In addition, the increase in the use of prescription opioids to treat pain has brought a significant public health problem in the form of substance abuse, addiction, and overdose deaths. The challenge is to understand pain better so as to treat it more effectively without the attendant public health risk posed by substance abuse.* (#134)

While some called for research toward the development of new drugs with less potential for abuse, others suggested attention to developing non-pharmaceutical interventions, such as prescription drug monitoring programs and eHealth records. One major point all respondents agreed on was the need for a greater amount of support to help solve this problem.

Food Addiction. Respondents perceived obesity, one of the three leading causes of preventable death, as an addiction to food. There was a call to better understand this behavioral disorder by evaluating existing research on food addiction and studying the addictive properties of food. Respondents identified the need for understanding:

- Obesity risk factors
- Reward and stress systems
- The control of food intake, especially addiction to high caloric foods
- The role of obesity as it contributes to chronic disease

One respondent thought it was important to develop new preventative and therapeutic options for obesity.

Pathological Gambling. Respondents were concerned with the growing problem of pathological gambling. The comorbid relationship between gambling and substance-related addictions and health problems was frequently cited as an area ripe for research.

> *Adult problem gamblers are five times more likely to have co-occurring alcohol dependence, four times more likely to abuse drugs, three times more likely to be depressed, eight times more likely to have bipolar disorder, three times more likely to experience an anxiety disorder and have significantly elevated rates of tachycardia, angina, cirrhosis.* (#395)

Calling for research on prevention and treatment, respondents emphasized the importance of understanding factors leading to recovery and resilience.

Addiction to Sex. Pointing to similarities between chemical addictions and hypersexual disorders (HD), respondents identified these disorders as a necessary area of research for the new institute. Respondents described a growing problem with pervasive negative outcomes.

> *As a licensed Marriage and Family Therapists and owner of a poly-addiction residential treatment center, I have concern over the high percentage of patients seeking help for HD who also have a substance use disorder and report abusing substances when seeking or engaging or recovering from their out-of-control sexual behaviors. Divorces were reported to be a direct consequence of their sexual addiction, especially cybersex or online out-of-control sexual behavior,* [which] *undermines family systems and has a larger impact on families and societies… Other* [reported problems] *include lost job productivity, comorbid health issues (e.g., depression, suicidal ideation, substance-related disorders, adult ADHD), and risk for unintended pregnancies. Collectively, individuals suffering from sexual addiction are in need of resources including empirically supported clinical protocols.* (#457)

Pointing to evidence of higher rates of sexually transmitted infections among those with HD, and fueled in part by our digital culture, respondents described HD as a public health issue in need of NIH support. Suggested areas for support included brain chemistry and pathways studies and the development of empirically-supported treatments.

Increased Risk of Disease (Theme 4)

The theme *Increased Risk for Disease* (*n*=47, 5%) is one of the original 13 areas of research.

- Understanding the mechanisms by which alcohol and other drugs of abuse increase risk for certain diseases (e.g., cancers), particularly when used in combination.

This theme captured comments in support of research that focused on the long-term, adverse health outcomes of drug and alcohol abuse. Repeatedly, respondents pointed to disease outcomes such as cancer, cardiovascular and respiratory problems, and kidney and liver failure.

> *We hope, as clinical investigators and clinicians, that a new combined institute would retain its focus on the medical complications of alcohol and other drug use, both those that occur among*

> *people with dependence diagnoses as well as those that occur with the much more common non-dependent forms of unhealthy substance use.* (#372)

Respondents recommended an integrated health model to study the broad effects of addiction and substance abuse on the physiological health of individuals, pointing to a diverse agenda of research topics as necessary to impact this issue.

A call to better understand the influence of genes on the effects of substance use was echoed by several respondents, with one respondent indicating the need for "a roadmap or specification emerging from the convergence of genetic and molecular information" (#470). Respondents also recommended a focus on the genetic and environmental influences that lead to addiction and the role of epigenetic mechanisms. Other recommended areas of study included:

- How substance withdrawal alters immune function and cancer susceptibility
- Effects of drug abuse on cardiovascular health, such as vessel stiffening and myocardial fibrosis
- Examination of the role of caffeine in glucose metabolism and the development of type II diabetes

The need for new and improved approaches to prevent and treat substance addiction in order to limit disease was highlighted.

Antecedents and Comorbidity (Theme 5)

In contrast to *Increased Risk for Disease*, which was about the long-term disease outcomes of substance abuse, this data-driven theme captured comments related to research on the causes and developmental progression of addictions, which included issues of comorbidity. *Antecedents and Comorbidity* (*n*=138, 14%) is about the relationship between behavioral or biological characteristics or conditions and the presence or development of drug abuse and addiction.

Identifying both mental and physical health problems that frequently co-occur with substance abuse, respondents repeatedly called for research on HIV/AIDS, hepatitis C, chronic pain, and mental health conditions, such as schizophrenia, post-traumatic stress disorder, anxiety disorders, depression, intimate partner violence, interpersonal abuse, and suicide. Beyond specific diseases or conditions, respondents noted the power of social and environmental factors in influencing substance abuse patterns and called for increased attention to issues of poverty, gender, criminal activity, and social and economic change as they relate to the development and persistence of substance abuse. In focusing on risk factors, causes, or comorbid conditions or behaviors, respondents differed in their opinion about which type of research was most important. For example, one respondent believed the comorbidity of substance abuse and mental health should be studied from a genetic perspective.

> *For instance, several recent studies have demonstrated that post-traumatic stress syndrome (PTSD) as well as exposure to assaultive trauma are heritable (see Stein et al., 2002) and at least 1 study has shown that this shared trait overlaps with risk for alcohol dependence (Sartor et al., 2011). This means that it is not just the simple idea that a person is exposed to trauma, gets PTSD*

> *and decides to "self-medicate" by drinking and using drugs but rather they have a shared genetic liability to all co-occur in that individual.* (#255)

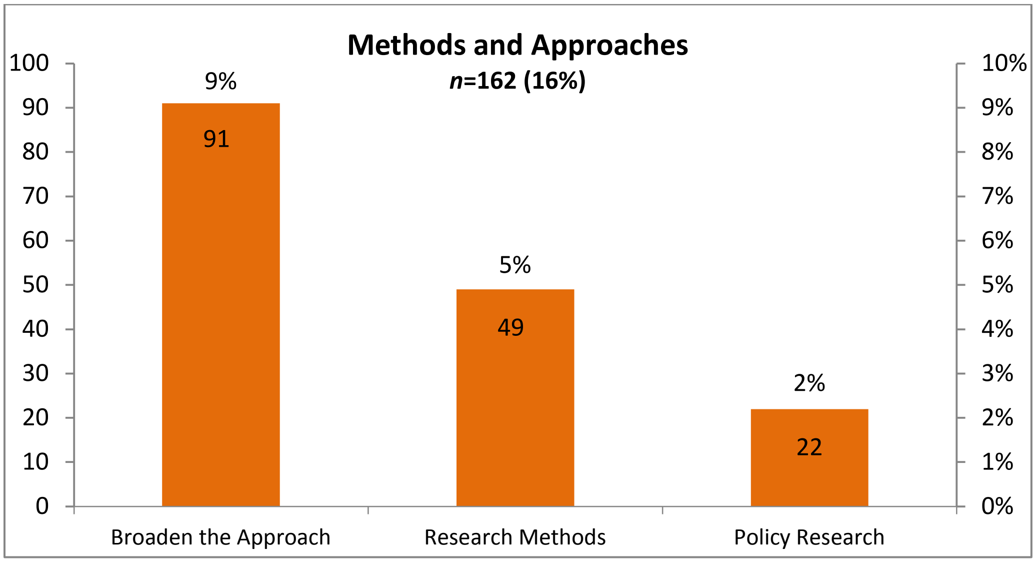
In contrast, another respondent emphasized the need to address substance abuse from a psychosocial perspective.

> *Research suggests that initiation of these behaviors is largely environmentally determined, and that socio-cultural environments (e.g., policy, peers, family) play pivotal roles in the initiation and, maintenance of, and desistence from drug use, abuse, and dependence. Certainly there is interplay of environmental and biological influences in the development of addiction, however, to downplay the social, cultural, and psychological aspects of substance use disorder is a fundamental exclusion that will severely weaken efforts at prevention and treatment, and diminish the national economic contribution of work supported by the new institute.* (#138)

Although comments were split on where research should concentrate, most recognized the complexity of human behavior and encouraged a multidisciplinary approach, which would include both the social and biological sciences (e.g., behavioral, developmental and policy research, epidemiology, and genetics).

Methods and Approaches (Primary Category 2)

The primary category *Methods and Approaches* focuses on the way in which respondents believed research at the new institute should be executed. The 162 comments in this primary category represent three themes: *Broaden the Approach* (*n*=91, 9%), *Research Methods* (*n*=49, 5%), and *Policy Research* (*n*=22, 2%). Together, the three themes described a call for more sophisticated and relevant research that would reflect real life, therefore enabling meaningful contributions toward informing public policy.



Broaden the Approach (Theme 6)

A data-driven theme, *Broaden the Approach* (*n*=91, 9%) encompassed the call for research on addiction using a holistic and multidisciplinary approach that includes perspectives beyond the individual substance. Respondents felt this was one of the main reasons for creating the new institute and urged NIH to continue recognizing addiction as a complex developmental problem. In contrast to *Antecedents and Comorbidity*, where respondents identified specific behavioral or biological characteristics or conditions as part of their call for greater involvement by the social sciences, *Broaden the Approach* captured a general call for a holistic approach, which would require both biomedical and psychosocial research. Echoed throughout these comments was the necessity of understanding substance abuse and addiction from all perspectives to identify all causes, build a comprehensive understanding of the phenomena, and offer effective solutions for treatment and prevention.

> *Research enterprises where behavioral science participated as a leader, or at minimum as an equal, have revolutionized the conceptualization of addiction-related problems (including obesity) and the development of efficacious interventions.* (#74)

While the majority of respondents asked for an increase in participation by the social sciences, and an approach that focused on multi-substance abuse, a few respondents asked for continued commitment to basic research, specifically the preservation of research in neuroscience and the genetics of addiction.

Research Methods (Theme 7)

Research Methods (*n*=49, 5%) emerged as a data-driven theme that captured comments calling for revised and improved methods and models for substance use, abuse, and addiction research. It included one of the original areas of research identified by the committee.

- Designing clinical trials that accurately reflect real-world conditions (e.g., greater inclusion of polydrug users)

Revised and Improved Methods. To advance knowledge about substance use, abuse and addiction, respondents suggested more support for advancing methodologies and using more complex research designs. Pointing to the importance of developing quantitative methods specific to a field of research, one respondent reflected on the infrequent focus on statistical methodologies used in alcohol research compared to other NIH-funded areas of research.

> *For example, in 2011, out of 19,113 publications on the topic of "alcohol", only 14 are in the "statistics and probability" category, of which a mere 2 (0.01%) papers were supported by NIAAA (data obtained from Web of Science). In comparison, 115 out of 18,403 papers on "AIDS", and 388 out of 98,679 papers on "cancer" are in the "statistics and probability" category. The odds ratio of the proportion of statistical papers is 8.6 for AIDS vs. alcohol (p<.00001), and 5.4 for cancer vs. alcohol (p<.00001).* (#112)

Also calling for improved methods for data structure and management, another respondent suggested the development of biospecimen banks for alcohol and drug disorders.

> *Well characterized brain specimens and/or biological fluids are difficult to find. This limitation has discouraged progress in the development of biochemical and "omic" biomarkers for these conditions since basic scientists have difficulty obtaining testable material.* (#279)

Still with a focus on the biology of addiction, respondents suggested better research design to reveal physiological and pathological mechanisms underlying addiction, the identification of molecular phenotypes resulting from drug exposure, and creation of technology that would link genetic and protein information to phenotypes of addictive behavior.

Respondents from the social sciences perspective called for research designs that could map addiction from early on. Noting that adult addiction could be tracked from early childhood based on particular risk factors, respondents suggested supporting research methods, such as longitudinal and natural history studies, to further understand the trajectory of abuse and addiction. Following the progression of substance use over time could potentially shed light on use patterns, treatment, relapse, co-occurring psychiatric disorders, and poly-drug interactions. Respondents believed this type of research would improve treatment and prevention options.

Real-World Clinical Trials. An original area of research identified by the committee, respondents agreed that clinical trials would be more effective if they reflected reality. Noting that comorbidity was often used to exclude individuals from clinical trials, and acknowledging the advantage of excluding comorbid factors to simplify analysis, respondents stated that real strides in treatment would only be made if research took into account the reality of an individual's actual situation.

Policy Research (Theme 8)

The theme *Policy Research* (*n*=22, 2%) is one of the original areas of research.

- Understanding the implications of Policy Research on substance use patterns and trajectories, especially in youth

Recognizing the impact public policy has on substance use, abuse, and addiction, respondents emphasized the critical need for the new institute to become more involved with informing policy. Studies that focus on understanding how policy facilitates prevention and inhibits substance use through laws that regulate taxes and pharmaceuticals were perceived to have the greatest potential impact on public health. One respondent noted the political complexity of these issues, pointing to the contradictions in our society about drugs and addiction.

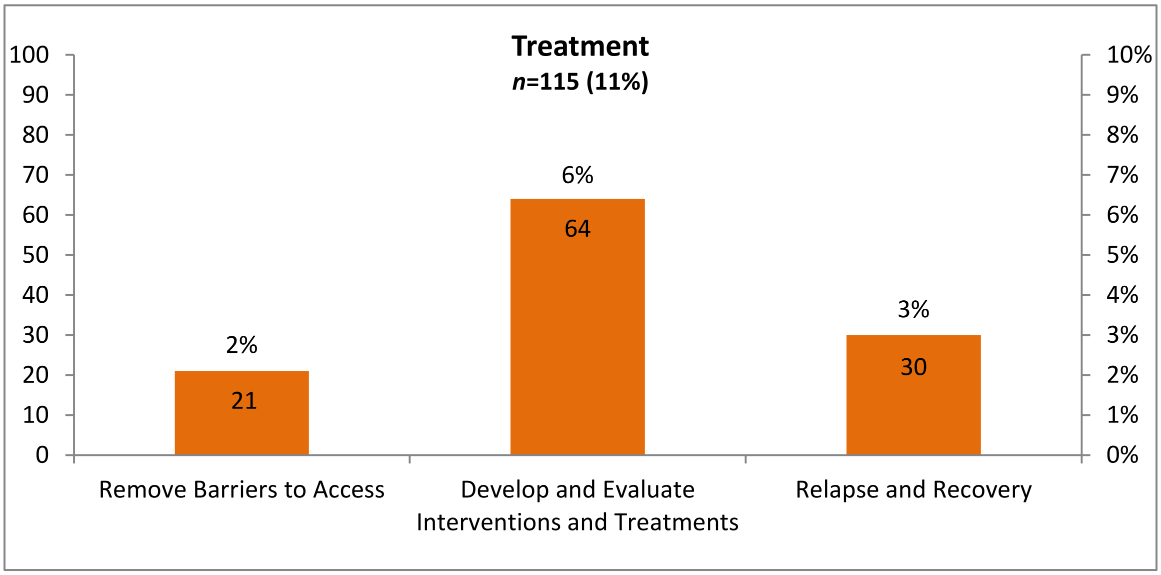
> *The policy arena radiates tension between inconsistent perspectives on the use of alcohol, tobacco and other drugs. Alcohol is a blessing and a curse. Opiates are valuable analgesics and illegal intoxicants. Possession and use of marijuana is a federal criminal offense that some states and communities ignore if the use is for medical purposes. Nicotine stimulates and relaxes; tobacco kills. Addiction is a brain disease; addicts are criminals. We seek to eliminate problems associated with the use and abuse of alcohol, tobacco and drugs while protecting the rights of industry to manufacture and market these products. Alcohol, tobacco and drug control policies in the United States are constructed from an admixture of state and federal legislation, voter referenda, judicial decisions, administrative regulations, local ordinances, program rules and practitioner licensing. The new institute must recognize that alcohol, tobacco, and drug use,*

> *misuse, and abuse reflect local, state, and federal policies and promote research to better understand how policy facilitates and inhibits the development and continuation of alcohol, tobacco, and drug use disorders and* [how policies] *can support prevention, treatment and recovery.* (#108)

Several respondents described a mismatch between the NIH mission statement and the areas of research identified in the RFI. Perceived as having too much focus on biological research, respondents were critical that NIH has failed to play a role in setting effective population-level policies that lead to a reduction in the negative consequences and public burden of addiction. Development of the new institute was perceived to signal an opportunity for NIH to take greater steps into the policy arena; respondents suggested greater support for policy and evaluation research.

Treatment (Primary Category 3)

The primary category *Treatment* captured 115 comments (11%) that called for the new institute to include a range of organizational support for research and other activities related to treating addictions and behavioral disorders. Specific comments related to treatment research for alcohol or tobacco use, abuse, and addiction were included in *Research Topics* (*Alcohol Use and Addiction*, and *Tobacco Use and Addiction*, respectively); the themes presented here are less substance-specific, and include more general and often systematic or programmatic needs. Three themes comprise this category: *Remove Barriers to Access* (*n*=21, 2%), *Develop and Evaluate Interventions and Treatments* (*n*=64, 6%), and *Relapse and Recovery* (*n*=30, 3%).



Remove Barriers to Access (Theme 9)

The theme *Remove Barriers to Access* (*n*=21, 2%) includes one of the original areas of research.

- Alleviating the translational bottleneck for treatments to move from the bench to the bedside to the community

Comments included support to alleviate the translational bottleneck that prevents treatments from reaching communities. Several respondents noted recent efforts to make translation a valued and necessary part of the research process for NIH-funded studies; carrying this over into the new institute was paramount for this group.

> *Type II translational research needs more explicit attention. We have so many programs that have proven to be effective and save money in the long run but we have yet to figure out how to get these programs disseminated widely. Gains in this area can have tremendous public health benefit.* (#44)

While the translational bottleneck was understood as part of the problem of getting research from the bench to the bedside, the flip side of the equation, getting individuals with substance abuse problems to the treatment, was also perceived as part of the problem. Often struggling with economic and/or psychological issues, respondents asked for research that focused on identifying and alleviating the barriers that keep individuals from seeking or accepting treatments. The National Association of State Alcohol and Drug Abuse Directors suggested that moving research from the bench to the bedside and into the community would be more effective if the new institute supported research on the dynamic interactions between prevention, treatment, and recovery.

Develop and Evaluate Interventions and Treatments (Theme 10)

Develop and Evaluate Interventions and Treatments is a data-driven theme that captured 64 (6%) frequently lengthy and detailed responses with very specific recommendations. It also incorporated one of the 13 original areas of research:

- Encouraging patient recognition and utilization of effective substance abuse treatments

Respondents believed the new institute should provide more support for effective treatments that could be developed as the underlying causes of addiction are understood, and the instances of appropriate diagnoses are increased. As new treatments are developed, respondents called for a balance between medical (pharmacological) and psychosocial approaches; specifically, they noted the need for non-pharmacological treatments to circumvent the likelihood of prescription drug abuse and addiction in treated individuals. They also mentioned the need for improved behavioral treatments for tobacco addiction. The following treatment suggestions were recommended for study:

- Medical (pharmacological)
    - Prescription drugs that reduce the strength of addiction
    - Drugs that are active against more than one type of addiction
    - Epigenetic drugs and genetic-based treatments
    - Prescription drugs to treat overdose
- Psychosocial
    - Adaptive treatment

  - Contingency management strategies
  - Behavioral treatments to help smokers quit

Respondents noted that research on new treatments should take into account that different sub-populations may respond differently to treatments. Women, older adults, minorities, veterans, poly-drug users, people with different levels of dependence, and individuals with comorbidities such as HIV, would all benefit from treatments that could be tailored to the individual. Respondents emphasized the need to develop flexible treatment programs that could respond to individual characteristics, needs, and problems.

> *Complex community health problems, like substance use and abuse, require comprehensive, collaborative solutions in order to achieve benefit for the entire community or targeted population. Substance use and abuse is influenced at multiple levels and as such interventions must be broad-based, comprehensive and seek change at multiple levels.* (#37)

Respondents called for solid, evidence-based, rigorous science to determine which treatments work in the real world. Respondents emphasized using efficacy trials to test and evaluate treatments, economic analysis to maximize resource use, and implementation science to find the best ways to deliver effective treatments.

Respondents identified the following issues related to the delivery of effective treatments:

- Health services delivery strategies and problems
- Access to treatment and retention of patients
- The need to provide treatment in many settings (the community, the workplace, and in conjunction with primary care)
- The need to treat all addictions in an individual at once
- The role of mutual-aid models (support groups) to supplement other forms of treatment
- Retaining mothers in treatment programs while supporting the mother-child relationship
- The difficulties of engaging sub-populations, such as individuals with HIV/AIDS, for treatment (costs and accessibility)

Overall, respondents agreed that a comprehensive approach that engages all vested parties is necessary for providing the best treatment options.

Improve Patient Outcomes. This sub-theme captured comments that echoed a need to understand what deters patients from getting effective treatment. Respondents called for more research in this area and suggested possible topics to explore including:

- Stigma associated with certain types of treatments (such as methadone) even though they are effective
- Reluctance to adopt medically assisted treatment along with psychosocial interventions
- Poor dissemination and accessibility of effective treatments
- Complexities of accessing and treating patients with comorbidities

- Misconceptions, false hopes, and lack of accurate information

As cost effective treatment or prevention strategies, respondents recommended leveraging new technology with research on the use of smart phones for program support through text messaging, the efficacy of virtual support groups, secure messaging linked to electronic medical records, and internet programs, such as mHealth initiatives.

Relapse and Recovery (Theme 11)

In the *Relapse and Recovery* (*n*=30, 3%) theme, respondents urged NIH to charge the new institute with undertaking a systematic, empirical investigation of recovery from addiction. This theme incorporated one of the committee's areas of research, *Other Substance Use*.

- Encouraging research to elucidate the impact of using one substance (e.g., alcohol) on likelihood of relapse to other substances (e.g., other drugs).

Respondents asked that the new institute develop a science of recovery and relapse that includes both biological and psychosocial perspectives, but emphasizes the influence of external factors. Perceived as a chronic condition, recovery was described as an ongoing process, not a one-time goal.

> *Research is needed to understand longitudinally the multiple pathways to long-term recovery. As a person goes along his or her recovery path, they experience a life filled or refilled with work, a place to live, relationships, and activities in the community. Research should examine how a person integrates recovery into an expanding quality of life and the stages that this process happens at with a community/environmental perspective.* (#311)

Several respondents pointed to the importance of further understanding the factors that lead to relapse after a sustained period of recovery.

> *Little work has been done on the follow up community based care of people following intensive addiction therapy. The follow up programs with metrics for early warnings signs of relapse are most important for primary care or the medical home physician.* (#26)

Relapse and Recovery also captured comments related to crime and the connection between recovery and relapse and the criminal justice system. Pointing to the fact that substance abusers have often been incarcerated, respondents voiced concern about the point of release when incarcerated users re-enter the community without adequate support systems.

Recommendations about specific areas of research to emphasize included:

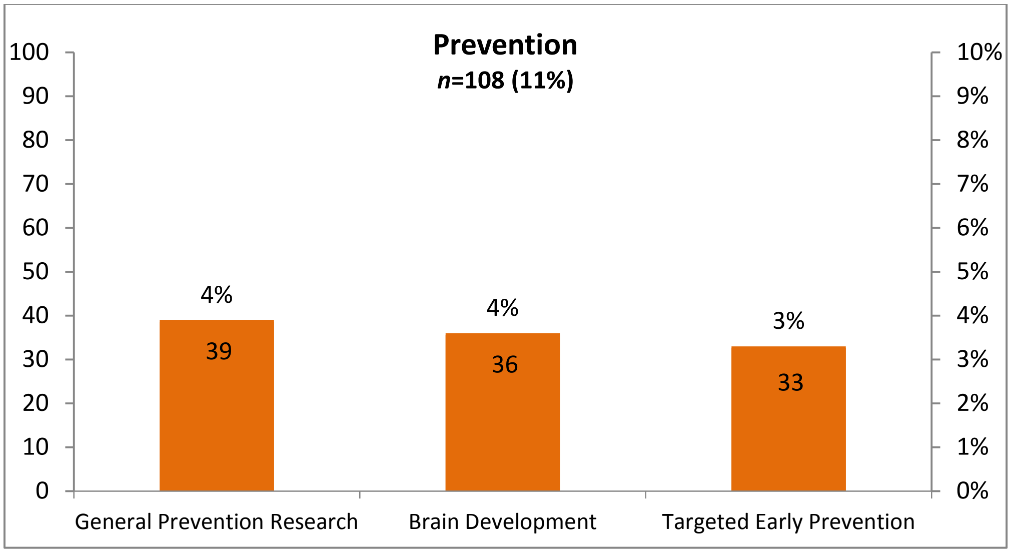
- Neurobiology of recovery and brain resilience
- Pathways, processes, stages, and styles of long-term recovery
- Role of benzodiazepines in recovery and relapse
- Need for better animal models for recovery science
- Impact of recovery on both physical and mental health
- Transition from treatment to community
- Role of family, community, peer groups, and other non-clinical recovery supports

- Self-management recovery
- Managed community-based care
- Recovery patterns and experiences for specific groups of people, including young people, women, and parents

Other Substance Use. A handful of respondents supported the inclusion of this original area of research in the new institute, noting that many substance abusers have multiple drug dependencies and may continue using some substances even when they no longer use others. Respondents suggested studies of the complex reward circuitry that may synergize dependencies, such as opioids and alcohol, and the role of gateway drug use (alcohol, tobacco, and marijuana) on relapse to other drugs.

Prevention (Primary Category 4)

The primary category *Prevention* captured 108 comments (11%) from respondents who were in support of increased organizational efforts on all aspects of prevention. Specific ideas related to prevention research for alcohol or tobacco use, abuse, and addiction were included in *Research Topics (Alcohol Use and Addiction*, and *Tobacco Use and Addiction*, respectively). The themes presented here are less substance-specific, and more about the importance of *General Prevention Research* (*n*=39, 4%), research on *Brain Development* (*n*=36, 4%) and *Targeted Early Prevention* (*n*=33, 3%).



General Prevention Research (Theme 12)

General Prevention Research (*n*=39, 4%) captured comments from respondents who strongly supported the continuation and promotion of prevention research in the new institute. Comments focused on alcohol, tobacco, and drugs, with less frequent mention of preventing behavioral disorders. They pointed out that from societal, humanitarian and economic perspectives, prevention is preferable to treatment and after-the-fact interventions.

Development of successful prevention strategies was recognized as inherently multi-dimensional. First, the many risk factors and underlying vulnerabilities that may lead to or promote substance use, as well as those that can reduce or mitigate it, need to be identified and their roles understood, individually and in combination. Respondents recommended prevention research in every area, from neurological (see *Brain Development*, theme 13) and behavioral studies, to sociological studies that explore the influence of social factors (e.g., gender, race, ethnicity, and sexual orientation) within different contexts (e.g., family, school, workplace, and community). One strategy toward prevention was to focus on at-risk populations, such as low-income individuals or those with HIV/AIDS, in an effort to target prevention programs. Respondents believed that successful prevention would require policy changes that could impact society as a whole.

Respondents noted that prevention of substance abuse and addiction should be seen as an on-going effort and not a one-time matter; first there is the ongoing need to prevent non-users from becoming addicted to substances, and then there is the ongoing challenge of preventing relapse after treatment. In addition to research that could inform prevention programs, policy research was also suggested as a key toward prevention efforts. Overall, respondents shared the opinion that the new institute should have a broad, comprehensive prevention portfolio.

Brain Development (Theme 13)

The following original area of research defined the theme *Brain Development* (*n*=36, 4%)

- Improving prevention efforts by developing a better understanding of the patterns and trajectories of drugs of abuse and their influence on brain development

Respondents highlighted the need for research about the direct effects of substances on the brain (neurobiology, reward circuits, brain remodeling, and brain structure, function, and connectivity), and the subsequent effects on behavior.

In addition to studying direct effects, respondents voiced support for understanding typical brain development. To examine the potential for early prevention before critical biological or behavioral changes occur, one respondent called for, “sophisticated longitudinal studies of typically-developing and high risk populations of children,” (#439). In addition, and as an alternative to the idea that drugs cause brain changes that lead to addiction, respondents supported investigating whether genetic predisposition influences substance use or addiction. The effects of substances on other organ systems may also be important and should be studied in conjunction with brain research.

Targeted Early Prevention (Theme 14)

The *Targeted Early Prevention* (*n*=33, 3%) theme represents the following original area of research:

- Targeting efforts to prevent substance abuse in adolescents and young adults

Respondents perceived early prevention efforts for adolescents and young adults as critical to reduce the magnitude and severity of addiction impacts on individuals and society. Evidence suggests that delaying age of first use reduces the risk of addiction.

> *By investing in research to define evidence-based practices for prevention, early intervention, and treatment of mental and substance use disorders as a public health priority, we will not only decrease societal costs and pressure on our current health care system, but we will also create healthier families, safer communities, and a stronger Nation.* (#501)

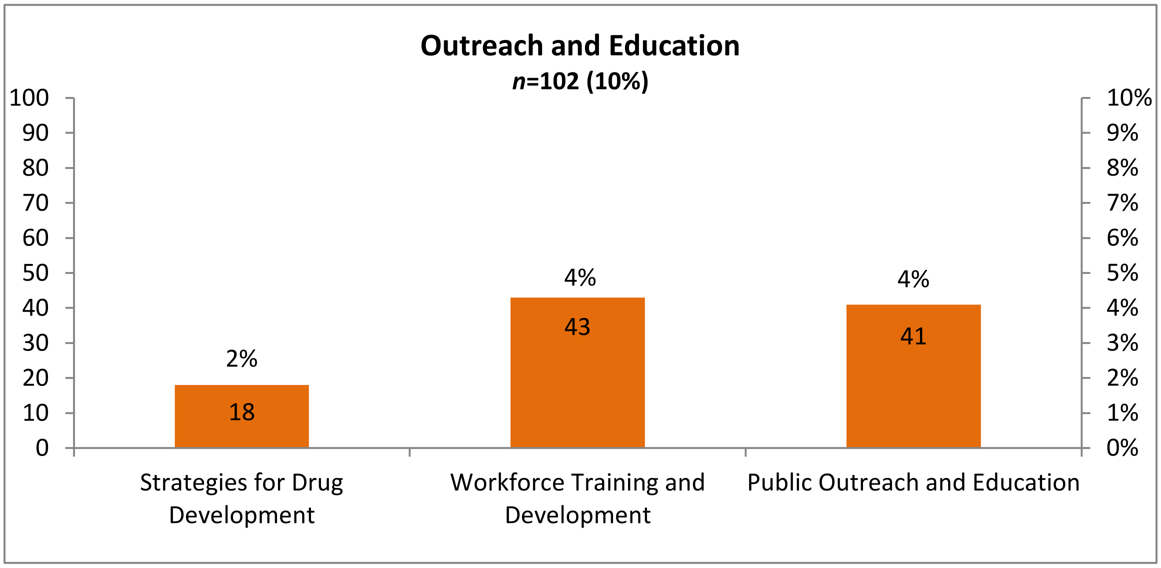
Several respondents described important ingredients for successful prevention efforts, including the need to go beyond the individual and permeate families, schools, and communities with prevention messages. Promoting positive behaviors and developing culturally-relevant and community-based programs were two other means toward early prevention.

From the research perspective, a primary message was that to deliver effective preventions, addiction had to be understood as a developmental disorder. Respondents reminded NIH of the continuum of substance use; that there is a progression from experimental use to abuse to addiction. Specific suggestions for research included studies focused on psychological vulnerabilities in adolescents, such as impaired control and impulsivity, as risk factors for later addiction. They also supported studies from different disciplinary perspectives, from neurobiological to behavioral, to understand how early substance use can lead to greater risk of addiction and mental disorders later.

While approaches to suggested prevention studies were primarily psychosocial, the possibility of developing vaccines or other medical interventions for adolescents that could prevent or reduce drug use was also suggested.

Outreach and Education (Primary Category 5)

Outreach and Education (*n*=102, 10%) captured sentiments related to the importance of having reliable and meaningful information available and delivered to the public; respondents believed communities needed and deserved support from the new institute. Three themes comprised this category: *Strategies for Drug Development* (*n*=18, 2%), *Workforce training and Development* (*n*=43, 4%), and *Public Outreach and Education* (*n*=41, 4%).



Strategies for Drug Development (Theme 15)

The theme *Strategies for Drug Development* (*n*=18, 2%) is one of the original areas of research identified by the committee:

- Developing strategies to enhance stakeholder interest in developing medications to treat various addictions, including nicotine and alcohol

Respondents recognized pharmaceutical companies were not engaged in developing drug treatments for addiction and suggested the new institute lead an organizational effort to engage them by encouraging and sponsoring the development of such medications. Specific suggestions to entice pharmaceutical companies to join the effort included:

- Grant orphan drugs status to treatments for illegal drug addiction (e.g., cocaine and amphetamines), to make it easier to gain patents and receive tax incentives.
- Extend patent protections to companies
- Encouraging industry-academic partnerships
- Increase the number of targeted requests for applications to encourage small businesses to develop drugs for addiction and substance abuse

Respondents stated NIH should work with the Food and Drug Administration to develop criteria for approval of new medications and off-label usage of approved drugs.

Workforce Training and Development (Theme 16)

Workforce Training and Development (*n*=43, 4%) included comments about training the current workforce and developing a future workforce that will be more capable of identifying, treating and preventing addiction and substance abuse. It encompasses the following committee-identified issue:

- Engaging the medical community in prevention and treatment of drug addiction and alcoholism

The consensus was that improving education and training efforts would be fundamental for reducing the public health burden of addiction. Comments fell into two broad groups, a larger one about training the practitioner workforce and a smaller one about training the research workforce.

Practitioners. Respondents strongly supported improved and expanded training programs for all personnel who deliver addiction and substance abuse services. Based on the commonly shared opinion that more and better trained staff is necessary at all professional levels, respondents specifically identified better training for physicians, psychologists, public health officials, and primary health care providers. Several respondents suggested an integration of primary medical care with the delivery of addiction services. Collectively, respondents described training a web of knowledgeable professionals in multiple fields, including health and human services, education, and the criminal justice system. Citing the view that the current system of training has not received sufficient validation or evaluation, several commenters recommended that training be based on the latest research findings and that there be a major effort to incorporate best practices. Respondents believed training should focus on evidence-based care and teach how to recognize, diagnose, treat, or refer individuals with addiction or substance abuse problems.

With regard to training physicians, there was a call for more training about addiction and substance abuse in medical school, but also as part of continuing education. Generally, respondents were concerned that the majority of physicians did not have the necessary knowledge or skills to effectively help patients presenting with symptoms; even worse, physicians were contributing to the problem.

> *Too many physicians prescribe narcotics as pain medications to recovering alcoholics and drug addicts, when other forms of pain relief might be available.* (#140)

Other recommendations for training the practitioner workforce included:

- Providing better information and resources (such as populations statistics) to general practitioners
- Training personnel who deliver recovery services to conduct self-evaluation
- Training or supporting clinicians to do addiction and substance abuse research
- Promoting collaborations between researchers and providers through conferences and workshops
- Using the synergy of the reorganization to develop well-integrated training programs

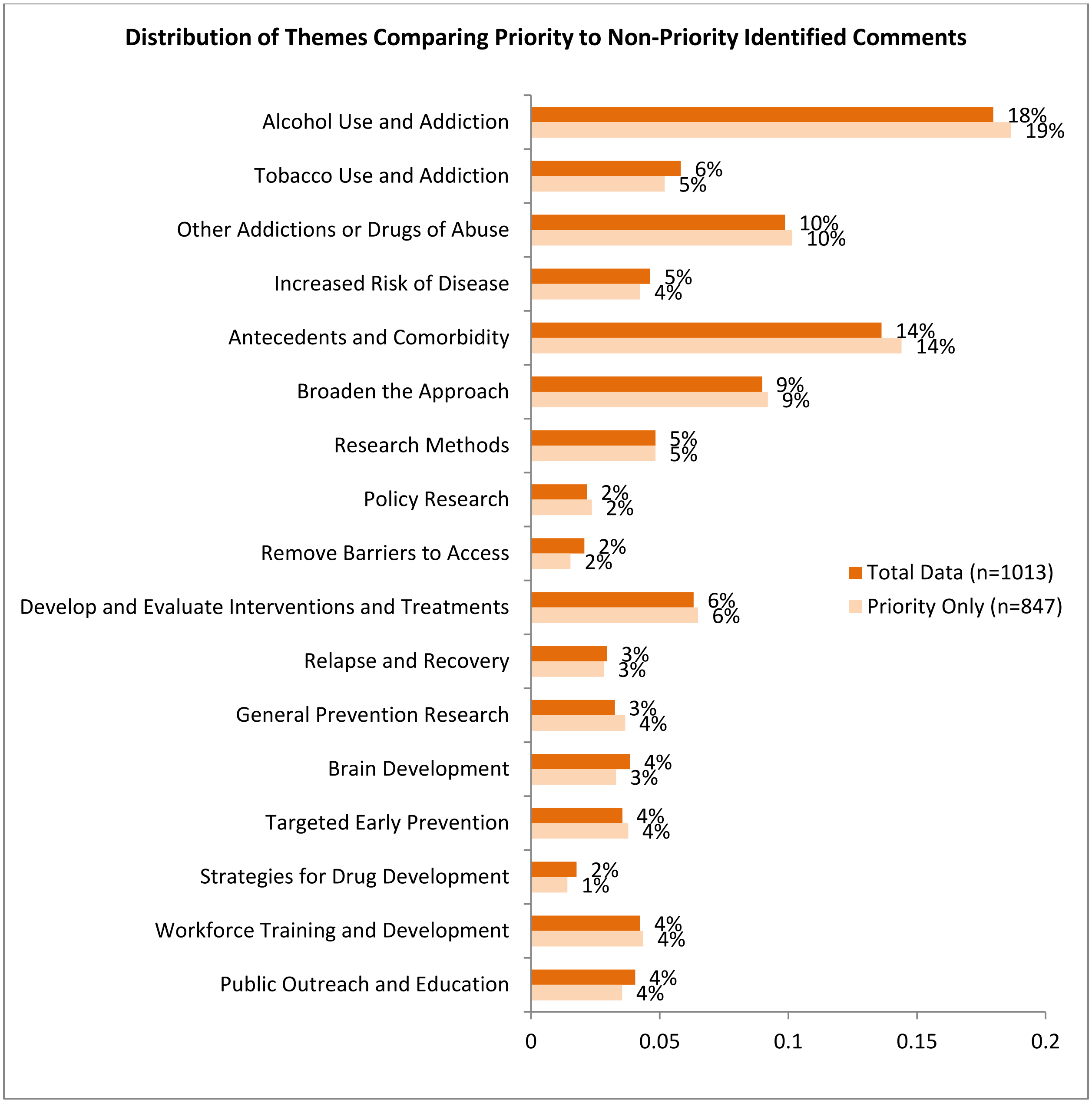
Research workforce. The over-riding issue raised by respondents who commented about the research workforce was the need to at least maintain the addiction research community. There was particular concern about supporting young investigators and maintaining a “pipeline” of researchers to replace those who retire or leave the field; one commenter recommended the use of targeted grant mechanisms. Respondents suggested encouraging and supporting training for individuals from diverse backgrounds and for those who are focused on population level research and translational studies (in addition to molecular biology, genetics and neurobiology). Training more clinicians to do research was also a common request. The research workforce was perceived as instrumental for determining what subject matter should be delivered and how to best deliver it.

Public Outreach and Education (Theme 17)

Public Outreach and Education (*n*=41, 4%) evolved from the data and captured comments related to raising public awareness about drug and alcohol use and addiction. Health promotion was an important piece of the puzzle for these respondents, who frequently suggested the use of public media and other means of communication to promote awareness. Noting the strength of social contexts for influencing substance use, social media was the most frequently mentioned avenue of communication (e.g., using Facebook for educating the public about the dangers of particular substances). Traditional ad campaigns and public service announcements were suggested, but not favored as strongly as the use of social media. Respondents also favored support for K-12 teacher training programs, and community outreach programs tailored specifically to minority or at-risk populations.

SECTION TWO: PRIORITY

The vast majority of comments (n=847, 84%) met the criteria for priority (see methods). The graph below illustrates a comparison of the distribution of themes across all comments versus priority comments. There was very little difference, and in both cases, the top three themes were *Alcohol Use and Addiction*, *Antecedents and Comorbidity*, and *Other Addictions or Drugs of Abuse*.



To give the planning committee an idea of how many people identified which themes as a priority (as opposed to the total number of extracted comments), we also assessed priority from an individual perspective. Of the 470 respondents who provided feedback to this RFI, 428 (91%) identified at least one theme as a priority. Three of the five *Research Topics* themes make up the first 3 of the top 5 priority themes. The top ten themes by priority are presented below; a complete table is provided in Appendix D.

Primary Category	Order of Priority by Theme	Number of Respondents (*n*=428)	Order of Priority
Research Topics	Alcohol Use and Addiction	159	1
Research Topics	Antecedents and Comorbidity	122	2
Research Topics	Other Addictions or Drugs of Abuse	86	3
Methods and Approaches	Broaden the Approach	80	4
Treatment	Develop and Evaluate Interventions and Treatments	56	5
Research Topics	Tobacco Use and Addiction	45	6
Methods and Approaches	Research Methods	43	7
Research Topics	Increased Risk of Disease	37	8
Outreach and Education	Workforce Training and Development	37	8
Prevention	General Prevention Research	33	9
Prevention	Brain Development	30	10
Outreach and Education	Public Outreach and Education	30	10

Priority of Issues by Affiliation

Regardless of affiliation, the themes in the top five match those of the themes identified by everyone in the dataset; however, a slight difference is found in how they are ordered. *Alcohol Use and Addiction* was the first priority among those who identified as “self”, while *Antecedents and Comorbidity* was priority one among those who identified as “organization.” Beyond the top five, those who identified as “organization” gave higher priority to *Relapse and Recovery* and *Targeted Early Prevention*, while those whose affiliation was “self” gave higher priority to *Tobacco Use and Addiction* and *Brain Development*. A full table of themes by order of priority is presented for both “self” and “organization” in Appendix D.

Conclusions

The five primary categories and 17 themes that resulted from the analysis of more than 1000 comments encompassed a wide range of topics and concerns. The majority of respondents provided feedback from an individual perspective. More than half of the comments suggested research topics that should be included in the scientific strategic plan; the rest of the comments were almost equally spread across the other four primary categories: *Methods and Approaches*, *Treatment*, *Prevention*, and *Outreach and Education*.

The three most frequently occurring themes fell under the primary category *Research Topics* and included *Alcohol Use and Addiction, Antecedents and Comorbidity,* and *Other Addictions or Drugs of Abuse*. *Broaden the Approach* (primary category *Methods and Approaches*) and *Develop and Evaluate Interventions and Treatments (*primary category *Treatment)* round out the top five most frequently occurring themes, which combined accounted for more than half of the total comments.

Respondents called for a better balance between support for biological and biomedical studies versus behavioral and psychosocial investigations related to substance use, abuse and addiction. Regardless of the area of research, a common message that cut across themes was the need for inter- and multidisciplinary research that recognized use, abuse, and addiction as a developmental problem with a complicated set of influences and outcomes.

In addition to the findings already discussed, a significant number of respondents chose to comment on the issue of resource allocation in the new institute, as well how the institute should be structured, managed, and conduct business. Many respondents expressed strong concerns about the total funding for the new institute, as well as allocation of funds between areas of research. Often, respondents suggested that the allocation of funding should match the public health burden of the identified research problem; most supported a diverse and balanced portfolio of research, with a corresponding balance of funding. Several commenters were concerned about disruption as a result of reorganization and called for a deliberate approach, with continuous monitoring of both progress and unintended consequences. We did not include these issues in the analysis because they were perceived as outside of the parameters of this RFI; however, the ideas were expressed with sufficient frequency to warrant mention.

In the context of the NIH mission, and pointing to the high economic and social costs of addiction at the individual, family, community, state, and global levels, respondents urged the NIH to support all efforts toward tangible outcomes with direct and positive influences.

Appendix

A. PLANNING COMMITTEE AREAS OF RESEARCH: TALLIES

Original Area of Research	*n*	%
Developing a compendium of the pharmacokinetic and pharmacodynamic interactions between alcohol and the therapeutics used to treat general medical and psychiatric conditions (e.g., hypertension, diabetes, epilepsy, depression)	6	1%
Encouraging research on the generation of novel metabolites resulting from the *in situ* interaction of alcohol with opiates, stimulants, hallucinogens, or inhalants (e.g., the production of cocaethylene when alcohol and cocaine are co-ingested) and their pharmacokinetic and pharmacodynamic properties and toxicity	4	0%
Understanding the mechanisms by which alcohol and other drugs of abuse increase risk for certain diseases (e.g., cancers), particularly when used in combination	47	5%
Developing strategies to enhance stakeholder interest in developing medications to treat various addictions, including nicotine and alcohol	18	2%
Engaging the medical community in prevention and treatment of drug addiction and alcoholism	20	2%
Encouraging patient recognition and utilization of effective substance abuse treatments	12	1%
Alleviating the translational bottleneck for treatments to move from the bench to the bedside to the community	21	2%
Improving prevention efforts by developing a better understanding of the patterns and trajectories of drugs of abuse and their influence on brain development	39	4%
Designing clinical trials that accurately reflect real-world conditions (e.g., greater inclusion of polydrug users)	15	1%
Encouraging research to elucidate the impact of using one substance (e.g., alcohol) on likelihood of relapse to other substances (e.g., other drugs)	9	1%
Targeting efforts to prevent substance abuse in adolescents and young-adults	36	4%
Understanding the implications of Policy Research on substance use patterns and trajectories, especially in youth	22	2%
Furthering knowledge of tobacco use and addiction, including co-morbidity with other addiction and psychiatric disorders	51	5%
	300	30%

B. CODING SCHEME: DESCRIPTION OF THEMES

The coding scheme evolved as an integration of committee-identified areas of research and data-driven ideas. The final coding scheme included 17 themes in five primary categories. The full coding scheme is provided below; we use symbols to identify which themes are committee identified areas of research (*), which are an integration of ideas from both the committee and the data ("+" = integration of one committee area, "ƚ" = integration of two committee areas), and which are strictly data-driven (no symbol).

RESEARCH TOPICS (PRIMARY CATEGORY 1)

ƚAlcohol Use and Addiction (Theme1): Furthering knowledge of alcohol use, abuse and addiction, including interactions of alcohol with other substances, fetal alcohol spectrum disorders and the need to broaden research approaches to alcohol-related research.

+Tobacco Use and Addiction (Theme 2): Furthering knowledge of tobacco use and addiction including comorbidities and behavioral interventions.

Other Addictions or Drugs of Abuse (Theme 3): Furthering knowledge of other drugs of abuse (not tobacco or alcohol) and addictive behavioral disorders; includes illicit drug use, addiction to prescription and over-the-counter drugs or products, hypersexual disorder, food addiction, and gambling.

+Increased Risk of Disease (Theme 4): Understanding the mechanisms by which alcohol and other drugs of abuse increase risk for certain diseases (e.g., cancers or other biological or epigenetic diseases), particularly when used in combination.

Antecedents and Comorbidity (Theme 5): Furthering knowledge about the relationship between behavioral or biological characteristics or conditions (risk factors) and the presence or development of drug abuse and addiction.

METHODS AND APPROACHES (PRIMARY CATEGORY 2)

Broaden the Approach (Theme 6): Research on addiction requires a holistic approach that goes beyond individual substances and recognizes addiction as a complex developmental problem with biopsychosocial influences; an increase in behavioral and interdisciplinary research is required.

+Research Methods (Theme 7): Develop methods that facilitate addiction research; use appropriate approaches for research design.

***Policy Research** (Theme 8): Understanding the implications of Policy Research on substance use patterns and trajectories, especially in youth.

TREATMENT (PRIMARY CATEGORY 3)

+Remove Barriers to Access (Theme 9): Improve understanding of, and remove barriers that both prevent people from accessing effective treatments, and also effective treatments from reaching the bedside.

+Develop and Evaluate Interventions and Treatments (Theme 10): Develop and evaluate interventions (e.g., models or programs, such as yoga, meditation, group therapy, leadership support, etc.) and treatments (e.g., medications) that are based on understanding the causes of addiction.

+Relapse and Recovery (Theme 11): Furthering knowledge about the factors and processes involved in the trajectories of recovery and relapse from individual, family, and community perspectives; develop and disseminate early warning signs for relapse after treatment.

PREVENTION (PRIMARY CATEGORY 4)

General Prevention Research (Theme 12): A general call to increase research on all aspects of prevention, including the development of programs based on local communities and empirically-tested strategies.

+Brain Development (Theme 13): Improving prevention efforts by developing a better understanding of the patterns and trajectories of drugs of abuse and their influence on brain development.

+Targeted Early Prevention (Theme 14): Targeting efforts to prevent substance abuse in adolescents and young adults

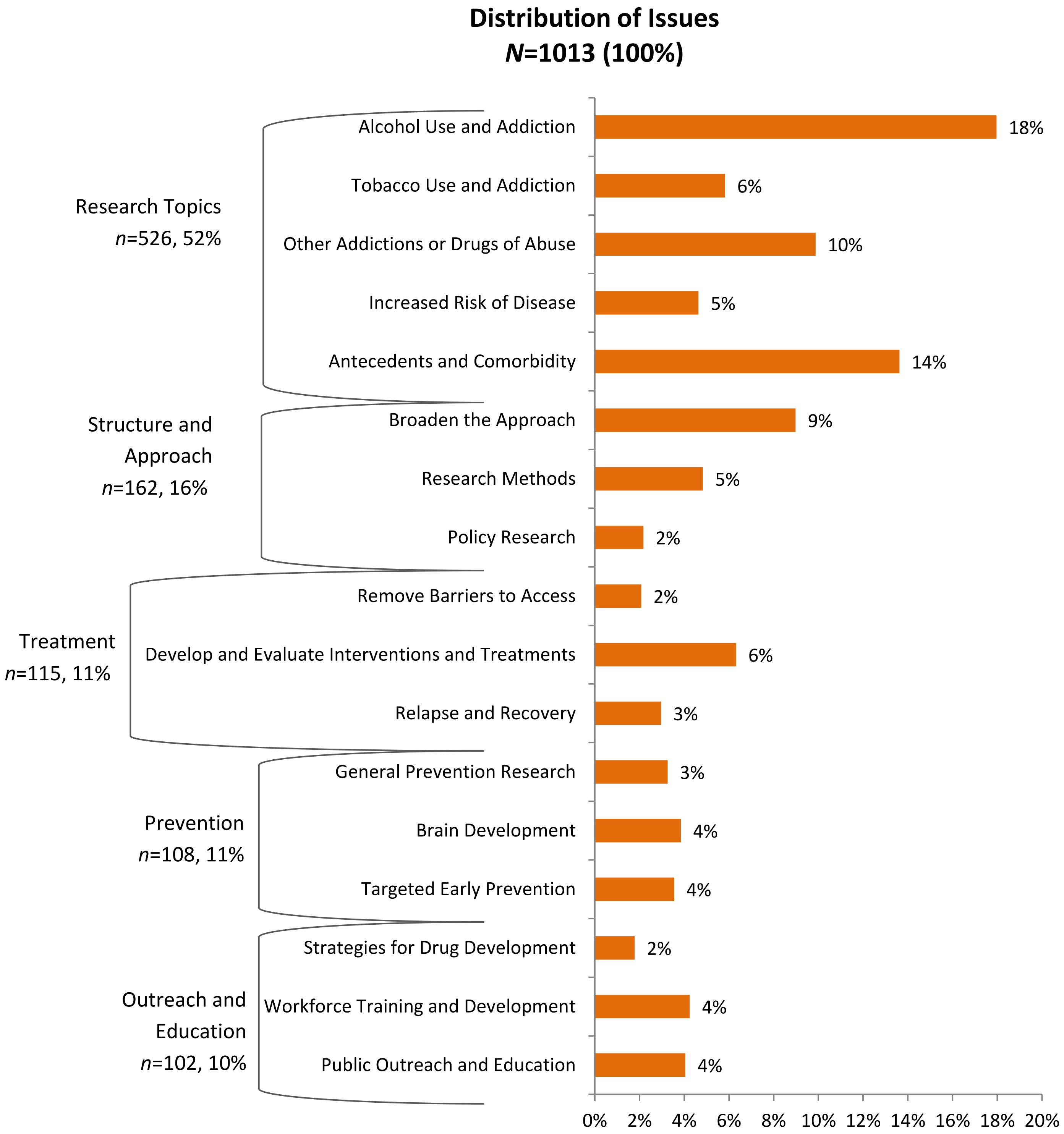
OUTREACH AND EDUCATION (PRIMARY CATEGORY 5)

***Strategies for Drug Development** (Theme 15): Developing strategies to enhance stakeholder interest in developing medications to treat various addictions, including nicotine and alcohol.

+Workforce Training and Development (Theme 16): Assist in developing the addictions workforce (clinicians, therapists, researchers, etc.), and provide data and materials to support training.

Public Outreach and Education (Theme 17): Raise public awareness about the outcomes of substance use, abuse, and addiction through social media, schools, parent groups, families, schools, and community groups; provide reliable information.

C. FREQUENCY DISTRIBUTION OF THEMES



D. PRIORITY OF THEMES

Total Respondents that Indicated Priority (*n*=428)

Primary Category	Order of Priority by Theme	Number of Respondents
Research Topics	Alcohol Use and Addiction	159
Research Topics	Antecedents and Comorbidity	122
Research Topics	Other Addictions or Drugs of Abuse	86
Methods and Approaches	Broaden the Approach	80
Treatment	Develop and Evaluate Interventions and Treatments	56
Research Topics	Tobacco Use and Addiction	45
Methods and Approaches	Research Methods	43
Research Topics	Increased Risk of Disease	37
Outreach and Education	Workforce Training and Development	37
Prevention	General Prevention Research	33
Prevention	Brain Development	30
Outreach and Education	Public Outreach and Education	30
Prevention	Targeted Early Prevention	29
Treatment	Relapse and Recovery	24
Methods and Approaches	Policy Research	20
Treatment	Remove Barriers to Access	13
Outreach and Education	Strategies for Drug Development	11

Respondents with "Self" Affiliation (*n*=343)

Primary Category	Order of Priority by Theme	Number of Respondents	Priority
Research Topics	Alcohol Use and Addiction	137	1
Research Topics	Antecedents and Comorbidity	97	2
Research Topics	Other Addictions or Drugs of Abuse	66	3

Primary Category	Order of Priority by Theme	Number of Respondents	Priority
Methods and Approaches	Broaden the Approach	59	4
Treatment	Develop and Evaluate Interventions and Treatments	42	5
Research Topics	Tobacco Use and Addiction	36	6
Methods and Approaches	Research Methods	32	7
Outreach and Education	Workforce Training and Development	28	8
Prevention	Brain Development	27	9
Research Topics	Increased Risk of Disease	27	9
Prevention	General Prevention Research	24	10
Outreach and Education	Public Outreach and Education	21	11
Prevention	Targeted Early Prevention	19	12
Methods and Approaches	Policy Research	17	13
Treatment	Relapse and Recovery	12	14
Treatment	Remove Barriers to Access	8	15
Outreach and Education	Strategies for Drug Development	7	16

Respondents with “Organization” Affiliation (*n*=85)

Primary Category	Order of Priority by Theme	Number of Respondents	Priority
Research Topics	Antecedents and Comorbidity	25	1
Research Topics	Alcohol Use and Addiction	22	2
Methods and Approaches	Broaden the Approach	21	3
Research Topics	Other Addictions or Drugs of Abuse	20	4
Treatment	Develop and Evaluate Interventions and Treatments	14	5
Treatment	Relapse and Recovery	12	6
Methods and Approaches	Research Methods	11	7
Research Topics	Increased Risk of Disease	10	8
Prevention	Targeted Early Prevention	10	9
Research Topics	Tobacco Use and Addiction	9	10
Prevention	General Prevention Research	9	10
Outreach and Education	Workforce Training and Development	9	10
Outreach and Education	Public Outreach and Education	9	10
Treatment	Remove Barriers to Access	5	11
Outreach and Education	Strategies for Drug Development	4	12
Methods and Approaches	Policy Research	3	13
Prevention	Brain Development	3	13